

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
20 September 2001 (20.09.2001)

PCT

(10) International Publication Number  
**WO 01/68098 A3**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/55**, A61P 35/00
- (21) International Application Number: PCT/US01/08480
- (22) International Filing Date: 15 March 2001 (15.03.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/189,699 15 March 2000 (15.03.2000) US
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
6 June 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/68098 A3

(54) Title: CEPHALOTAXINE ALKALOID COMBINATION COMPOSITIONS AND USES THEREOF

(57) Abstract: A method of treatment of a host with a cellular proliferative disease, comprising contacting the host with a cephalotaxine and an antiproliferative agent, each in an amount sufficient to modulate said cellular proliferative disease, is described. In some embodiments, the cephalotaxine comprises homoharringtonine (cephalotaxine, 4-methyl-2-hydroxy-2-(4-hydroxy-4-methyl pentyl) butanedioate ester). Antiproliferative agents of the invention comprise alkylating agents, intercalating agents, metal coordination complexes, pyrimidine nucleosides, purine nucleosides, inhibitors of nucleic acid associated enzymes and proteins, and agents affecting structural proteins and cytoplasmic enzymes.

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2002 JUN 17 AM 10:27

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/08480

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K31/55 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EMBASE, EPO-Internal, CHEM ABS Data, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	C. VISANI ET AL: "Effects of homoharringtonine alone and in combination with alpha interferon and cytosine arabinoside on "in vitro" growth and induction of apoptosis in chronic myeloid leukemia and normal hematopoietic progenitors" LEUKEMIA, vol. 11, 1997, pages 624-628, XP008000008 abstract  --- -/--	1,3,6, 10-14

☒ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

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Date of the actual completion of the international search

7 March 2002

Date of mailing of the international search report

22/03/2002

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Int. .tional Application No  
PCT/US 01/08480

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBASE 'Online! ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; YUZHU Z. ET AL: "Homoharringtonine, cytarabine and aclarubicin (HAA) combination chemotherapy for acute myeloid leukemia (AML)." retrieved from STN Database accession no. 1998384948 XP002192356 abstract &amp; CHINESE JOURNAL OF CLINICAL ONCOLOGY, (1998) 25/10 (758-759). ,</p>	1,3,6, 10-14
X	<p>DATABASE EMBASE 'Online! ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; LASTER JR. W.R. ET AL: "Therapeutic synergism (TS) of homoharringtonine (H) plus 5-fluorouracil (FU) against leukemia P388 (P388/O) and ARA-C-resistant P388 (P388/ARA-C)." retrieved from STN Database accession no. 82182588 XP002192357 abstract &amp; PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, (1982) VOL. 23/- (NO. 786). CODEN: PAACA3,</p>	1,3,6, 10-14
X	<p>ZHANG ET AL: "Inhibitory effects of homoharringtonine and hydroxycamptothecin in combination with other agents on cancer cell growth" ASIA PACIFIC JOURNAL OF PHARMACOLOGY, SINGAPORE UNIVERSITY PRESS, SG, vol. 7, 1992, pages 191-195, XP002112006 ISSN: 0217-9687 page 194, right-hand column abstract</p>	1,3,6, 10-14
A	<p>TAKANO I ET AL: "Ester-type cephalotaxus alkaloids from cephalotaxus harringtonia var. drupacea" PHYTOCHEMISTRY, PERGAMON PRESS, GB, vol. 44, no. 4, February 1997 (1997-02), pages 735-738, XP004292875 ISSN: 0031-9422 the whole document</p>	1-14
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International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>TAKANO I ET AL: "NEW OXYGENATED  CEPHALOTAXUS ALKALOIDS FROM CEPHALOTAXUS  HARRINGTONIA VAR. DRUPACEA"  JOURNAL OF NATURAL PRODUCTS, XX, XX,  vol. 59, no. 12, December 1996 (1996-12),  pages 1192-1195, XP000990654  ISSN: 0163-3864  abstract</p>	1-14

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